REMARKS

Claims 1-18 are pending. Claims 1, 11, 17 and 18 have been amended. No new subject matter has been added.

Rejection Under 35 U.S.C. § 102(b):

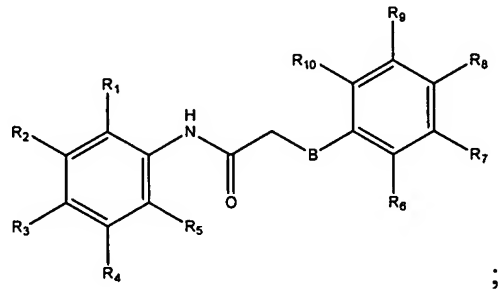
Claims 11, 12 and 17 stand rejected under 35 U.S.C. § 102(b) for allegedly being anticipated by Wright et al., J. Med. Chem., 2001, 44, 3187-3194 (hereinafter "Wright"). Wright discloses compounds that are derivatives of cryptolepine, an alkaloid comprised of four fused rings, which are potent antiplasmodials, and therefore potentially useful as antimalarial agents. The Examiner specifically points to compounds of formula 17 on page 3188, which are intermediates in the formation of the desired products.

In order for a claim to be anticipated under 35 U.S.C. § 102, a prior art reference must disclose each and every limitation recited in the claim. Claims 11, 12 and 17 are directed to compositions for the treatment of hepatitis, not individual compounds. Therefore, these claims cannot be anticipated by a reference that only discloses a compound, but does not disclose the composition containing it and how to make the composition. Moreover, Wright does not disclose that these compounds are useful in treating inflammation or inflammatory diseases, let alone hepatitis, which the compositions of the present invention are specifically directed to. Nor is there any disclosure in Wright that the intermediate compounds even possess biological activity, not even antiplasmodial activity, which is the focus of the article. Wright clearly does not disclose pharmaceutical compositions containing these compounds, which is what is claimed in present application. To make this difference abundantly clear, Applicants have amended composition claims 11 and 17 to add the phrase "and a pharmaceutically acceptable carrier"

solely to advance prosecution.[1] Therefore, Applicants respectfully submit that the present claims are not anticipated by Wright, since it does not teach all the limitations of those claims and respectfully ask that this rejection be withdrawn.

Rejection of Claims 11-14, 17 and 18 Under 35 U.S.C. § 103(a):

Claims 11-14, 17 and 18 stand rejected under 35 U.S.C. § 103(a) for allegedly being obvious over U.S. Patent No. 5,741,926 (the '926 patent). The '926 patent discloses compounds of the following formulas:



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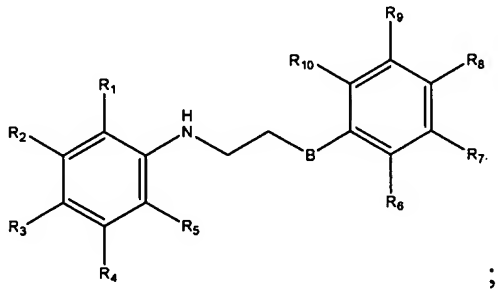
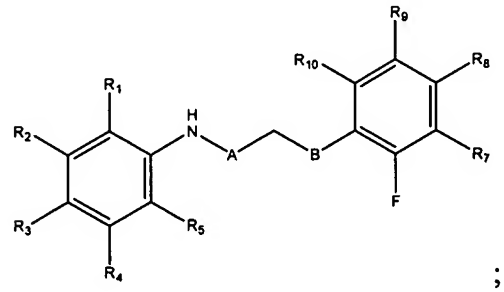


; and



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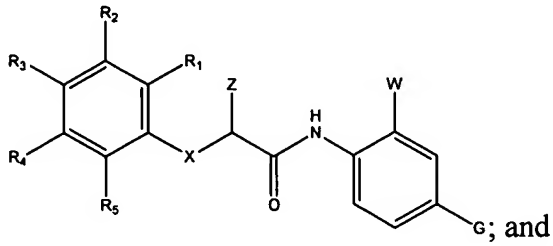
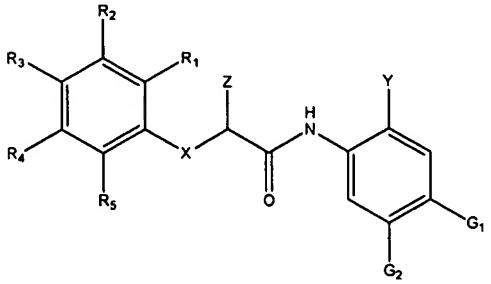
[1] Claim 11 also has been amended to correct a self-evident typographical error ("tertrazolyl" should be –tetrazolyl--).

wherein A is CH_2 or C(O), B is O, S, NH, R_6-R_{10} can be H, -OH, alkoxy, -SH, -S-alkyl, alkyl or Ph, and one of R_1-R_5 can be COOH or tetrazolyl. Whereas the present invention discloses method of treating hepatitis C using compounds of the formulas:

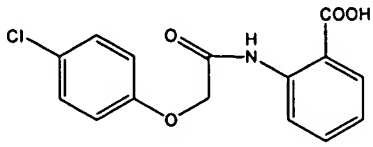


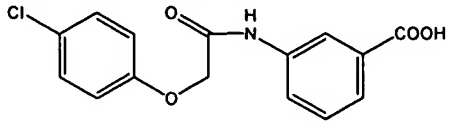
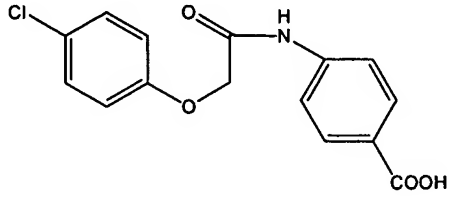
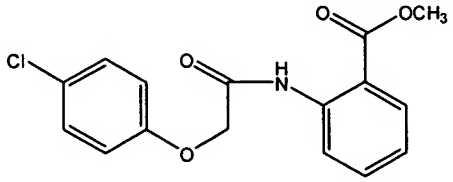
; and



wherein R_1-R_5 can be H, halo, Me, Et, CH_3O, NO_2, alkenyl, CN and CF_3, X is O, S, NH or NR, Z is H or CH_3, W is COOH or S-tetrazolyl, G is OH, F or H, G_1 is OH, F, CH_3O or H, G_2 is H, OH, Cl or CH_3O, and Y is COOH or CO_2CH_3. The present claims are also directed to pharmaceutical compositions for treating hepatitis C containing compounds of these formulas. Therefore, the major differences in structure is that the present invention teaches the importance of having either a COOH, $COOCH_3$ or 5-tetrazolyl group at the 2-position of the phenyl ring and that additional substituents on this ring should be at the 4 or 5-position.

In fact, the Applicants have synthesized and tested the following compounds:

Compound	IC_{50} for CHV Polymerase
	1.6 μM

Compound	IC_{50} for CHV Polymerase
	> 33 μM
	> 29 μM
	> 31 μM

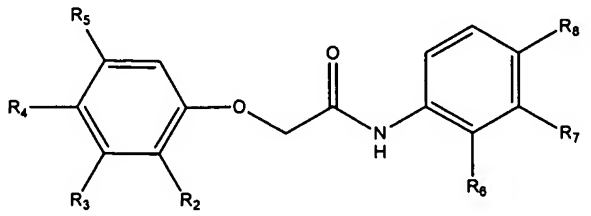
As can be plainly seen from viewing the above activity of these compounds, which are structurally substantially the same except for the positional substitution of the carboxyl acid functional group, the ortho-substituted isomer is far more potent in inhibiting HCV polymerase than the meta- and para-substituted analogs. The '926 patent does not teach or suggest the importance of having the carboxyl acid function group, or a methyl ester thereof, at ortho position. Nor does it teach or suggest that having a 5-tetrazolyl group at the ortho position also increases the potency of the compound relative to the meta- and para-substituted analogs. Thus, this dramatic increase in potency due to the substitution at the ortho-position of the right side phenyl ring is clearly a surprising result. For this reason, claims 11-14, 17 and 18 are patetentable over the '926 patent.

Moreover, the '926 patent does not teach or suggest that the compounds disclosed therein are potent inhibitors of HCV polymerase or in anyway possess any anti-hepatitis activity. In contrast, claims 11-14, 17 and 18 of the present application clearly indicate the pharmaceutical composition claims are useful for the treatment of hepatitis C.

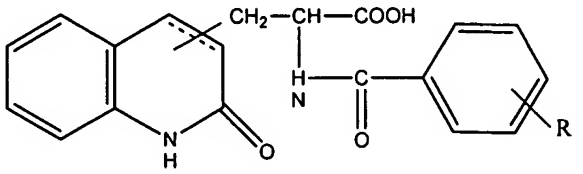
Accordingly, Applicants respectfully submit that claims 11-14, 17 and 18 of the present application are not obvious in view of the disclosure of the '926 patent, and respectfully request that this rejection be withdrawn.

Rejection of Claims 1 and 15 Under 35 U.S.C. § 103(a):

Claims 1 and 15 stand rejected under 35 U.S.C. § 103(a) for allegedly being obvious over Ryznerski et al. ("Ryznerski") in view of U.S. Patent No. 5,637,597 ("the '597 patent"). In Ryznerski, the Examiner points to the disclosure of compounds of formula (I-XVII):



wherein R_6 can be COOH, R_8 can be OH and R_2-R_5 can be alkyl, Cl or Br. These compounds are indicated to be inhibitors of prostaglandin synthetase, an enzyme involved in the inflammation pathway. The '597 patent discloses compounds of the formula:



wherein R is halo, and that these compounds inhibit the production of interleukin-8 and granulocytes activation, and therefore may be useful to treat inflammatory diseases.

Present claims 1 and 15 are directed to methods of using the compounds disclosed in the specification to treat hepatitis. The Examiner contends that one skilled in the art would be motivated to combine Ryznerski and the '597 patent to arrive at the methods of claims 1 and 15. The Examiner relies on the compounds disclosed in Ryznerski, as well as the disclosure in the '597 patent that its compounds possess activity that make them useful in the treatment of

inflammatory diseases and that hepatitis is one of the many diseases classified as an inflammatory disease. Applicants, however, respectfully disagree with this analysis for the following reasons.

First, the compounds disclosed in Ryznerski are substantially different in structure from those disclosed in the '597 patent, and the compounds are disclosed for different therapeutic purposes. At least for, Applicants respectfully submit that one of ordinary skill in the art would not be motivated to combine the teaching of these two references.

Secondly, even assuming for argument's sake that one of ordinary skill in the art would have been motivated to combine these reference based upon the structures of the compounds, Applicants do not believe that a skilled artisan would have a reasonable expectation of success. This is because the category of "inflammatory disease" encompasses a very large number of diseases, which act through many different pathways. As an example, the compounds disclosed in Ryznerski are inhibitors of prostaglandin synthetase, while the compounds disclosed in the '597 patent inhibit the production of interleukin-8 and granulocytes activation. The '597 patent lists fifteen different sub-categories of inflammatory diseases alone, and specifies that this is not to be considered an exhaustive list. Applicants respectfully assert that common sense alone should inform the average person of ordinary skill in the art that one molecule, or one family of molecules, cannot possibly be able to treat so many different diseases that act through so many different pathways. The compounds of the '597 patent are active in inhibiting the production of interleukin-8, but there is absolutely nothing to suggest that they can be used to treat hepatitis. The skilled artisan cannot have a reasonable expectation, simply because a certain molecule, or family of molecules, is useful in treating one inflammatory disease, that it will also be useful in the treatment of other unrelated inflammatory diseases. For example, it is well

known that there is no one compound capable of treating all kinds of cancer. One of ordinary skill in the art would also know that human papillomavirus (HPV) is a viral family that includes over 100 different types, and that no one drug can treat all types (as an example, on June 8, 2006, the Food and Drug Administration approved a vaccine, but it was only approved for the indication of providing protection against infection by HPV types 16, 18, 6 and 11). Also, when being treated for HIV, patients are typically dosed with "drug cocktails" containing 2 or 3 different drugs due to this virus's propensity to mutate. Thus, one of ordinary skill in the art would have been aware that one drug cannot effectively treat all related viral infections or cancers. Clearly, it would be highly speculative to conclude one anti-inflammatory agent to be effective against such a wide range of disease as recited in the '597 patent.

There is even more uncertainty when speculating whether one anti-inflammatory agent would also be effective in treating the same diseases as another anti-inflammatory agent when the other anti-inflammatory agent is structurally different and/or works via a different mode of action. Therefore, Applicants respectfully suggest that one of ordinary skill in the art would not be motivated to combine these references to arrive at the claimed invention. Applicants respectfully submit that no skilled artisan would have had a reasonable expectation that every anti-inflammatory agent would be effective in treating hepatitis C. For example, physicians do not prescribe aspirin and ibuprofen, which are both commonly used anti-inflammatory agents, to treat hepatitis C.

For the foregoing reasons, Applicants respectfully submit that claims 1 and 15 are not obvious over Ryznerski and the '597 patent and respectfully request that this rejection be withdrawn.

Amendment of Claims 1 and 18:

Claim 1 has been amended to correct a self-evident typographical error ("tertrazolyl" should be –tetrazolyl--).

Claim 18 also has been amended to correct an error. Claim 18 is dependent from claim 17, which is directed to a pharmaceutical composition. Thus, claim 18 should likewise be directed to a pharmaceutical composition, not a method. Accordingly, the language of claim 18 was amended to correct this error. Support for this amendment can be found on page 7 specifically, and throughout the present specification generally.

Applicants respectfully submit that present application is in condition for allowance and respectfully request favorable re-consideration and allowance.

Applicants' undersigned attorney may be reached in our New York office by telephone at (212) 218-2100. All correspondence should continue to be directed to our address given below.

Respectfully submitted,

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